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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,956	10/05/2007	Hyun-Ah Kang	HANOL-13037	2242

72960 7590 07/06/2009
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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
07/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,956	KANG ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 October 2007* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action
Election/Restrictions

Applicant's election without traverse of species α-1,2-mannosidase and *Saccharomyces cerevisiae* invertase, in the reply filed on 04/22/09 is acknowledged. Claims 1-11 are pending in this application for examination and are now under consideration.

Priority

This application is a 371 of PCT/KR04/01819 filed on 07/21/2004 and claims the priority date of Korea application 10-2004-0006352 filed on 01/30/2004. Examiner notes that the applicants have provided a certified copy of Korea application 10-2004-0006352 filed on 01/30/2004, however no English translation of said application has been provided. Therefore, the priority date for instant claims under consideration is deemed to be the filing date of the instant application filed on 07/21/2004.

Specification-Objection
Sequence Compliance

Applicants are advised that the application is not in compliance with 37 CFR §§ 1.821-1.825. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825. Specifically, applicants are required to comply with the sequence rules by inserting the sequence identification numbers of all sequences within the claims and /or specification. It is particularly noted that Fig. 1 and 2 are sequences, but applicant fails to provide the SEQ ID NO: (sequence identifier) to these sequences either in the figures or in the figure description. Sequences must be referred to by their

sequence identifiers, see particularly 37 CFR 1.821(d). If the sequences appearing in the specification do not have SEQ ID NO: assigned to them, then an amendment to the sequence listing will be required as well. There must not be any new matter submitted, therefore it is important to be careful to include only the sequences that are already disclosed in the current specification. Failure to correct the deficiency will be held a non-responsive to this Office action.

Claim Rejections: 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3 are rejected under 35 U.S.C. 101, because the claim reads on non-statutory subject matter. Claims 1 and 2 are drawn to "A nucleic acid...", and claim 3 is drawn to "A protein..." which reads on the product of nature. Claims directed to such subject matter are considered non-statutory because they read on products of nature. Examiner suggests amending the claim to recite "An isolated nucleic acid..." and "An isolated protein...", to show the hand of man, in order to overcome the rejection. Appropriate correction is required.

Claim Rejections 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 is indefinite in the recitation of "production of a recombinant glycoprotein with reduced glycosylation", the metes and bounds of the claim are not clear to the examiner, since claim does not recite structural features/patterns of glycosylation and compared to what reference glycosylation pattern the reduction is being compared to? As "glycosylation" and "reduced" are relative terms. Clarification and correction is required. For examination purposes examiner considers the phrase to mean any glycosylation pattern and said glycosylation pattern is reduced to any extent.

Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide having α-1,6-mannosyltransferase activity and comprising the amino acid sequence of SEQ ID NO: 2 and encoded by a polynucleotide of SEQ ID NO: 1; a specific *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising polynucleotide sequence encoding a α-1,2-mannosidase having the activity of synthesizing sugar chains with 5 or 6 mannose residues, said polynucleotide sequence isolated from the nucleic acid of *Aspergillus saitoi* by PCR amplification using the primers of SEQ ID NO: 13 (forward primer) and SEQ ID NO: 14 (reverse primer) and said engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP; comprising a specific mutation) transfected with an expression vector comprising

polynucleotide sequence encoding a α-1,2-mannosidase capable of producing glycoproteins comprising human mannose-type N-glycan (Example 5, pages 24-27 of specification), does not reasonably provide enablement for: i) any nucleic acid molecule encoding a polypeptide having α-1,6-mannosyltransferase activity and comprising an amino acid sequence having at least 90% homology to the amino acid sequence of SEQ ID NO: 2 (as in claims 1-3); and ii) an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern (as in claims 4-11). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

The breadth of the claims: Claims 1-11 are so broad as to encompass : i) any nucleic acid molecule encoding a polypeptide having α-1,6-mannosyltransferase activity

and comprising an amino acid sequence having at least 90% homology to the amino acid sequence of SEQ ID NO: 2 (as in claims 1-3); and ii) an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern (as in claims 4-11). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to extremely large number of polypeptides and encoding polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function.

The amount of direction or guidance presented and the existence of working examples: The specification is limited to teaching the use of an isolated polypeptide having α-1,6-mannosyltransferase activity and comprising the amino acid sequence of SEQ ID NO: 2 and encoded by a polynucleotide of SEQ ID NO: 1; a specific *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising polynucleotide sequence encoding a α-1,2-

mannosidase having the activity of synthesizing sugar chains with 5 or 6 mannose residues, said polynucleotide sequence isolated from the nucleic acid of *Aspergillus saitoi* by PCR amplification using the primers of SEQ ID NO: 13 (forward primer) and SEQ ID NO: 14 (reverse primer) and said engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP; comprising a specific mutation) transfected with an expression vector comprising polynucleotide sequence encoding a α-1,2-mannosidase capable of producing glycoproteins comprising human mannose-type N-glycan (Example 5, pages 24-27 of specification), but provides no guidance with regard to the making of other variants and mutants of SEQ ID NO: 2 with α-1,6-mannosyltransferase or an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (for example, see Whisstock et al., Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003, Aug. 36 (3): 307-340. Review), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polypeptides and encoding polynucleotides encompassed by these claims.

The state of prior at, the relative skill of those in the art, and the predictability or unpredictability of the art: While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is not routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claim, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions or deletions.

It is also noted that the art teaches several examples of how even small changes in structure can lead to changes in function. For example, Witkowski et al. (Biochemistry, 1999, Vol. 38: 11643-116150) teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol., 2001, Vol. 183 (8): 2405-2410) teaches that two naturally occurring *Pseudomonas* enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function.

Claims 1-11 as written are directed to random variant and mutant polypeptides having 90% homology to SEQ ID NO: 2 with α-1,6-mannosyltransferase or an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP)

transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern, would clearly constitute **undue** experimentation.

The quantity of experimentation required to practice the claimed invention based on the teachings of the specification: Additionally, Guo et al., (PNAS, 2004, Vol. 101 (25): 9205-9210) teach that the percentage of random single-substitution mutations, which inactivate a protein, using a protein 3-methyladenine DNA glycosylase as a model, is 34% and that this number is consistent with other studies in other proteins (page 9206, paragraph 4). Guo et al., (*supra*) further show that the percentage of active mutants for multiple mutations/changes appears to be exponentially related to this by the simple formula $(0.66)^{x}$ X 100% where **x** is the number of mutations introduced (Table 1, page 9206). Applying this estimate to the protein recited in the instant application, 90% homology to amino acid sequence of SEQ ID NO: 2 allows up to 43 mutations/changes within the 428 amino acid residues of SEQ ID NO: 2 and, thus, only $(0.66)^{43}$ X 100% equivalent to **1.7×10^{-6} %** of random mutants and having 90% homology to amino acid sequence of SEQ ID NO: 2 would be active. While these calculations are only estimates of the actual situation, they are presented to provide a basis for understanding the examiner's decision on which claim scope would require only routine experimentation and which claim scope would reach a level which is undue. The guidance in the instant case and current techniques in the art (i.e., high throughput mutagenesis and screening techniques) would allow for finding a reasonable number of

active mutants within about a hundred thousand inactive mutants of SEQ ID NO: 2. But finding a few mutants within several millions or more, as in the claims to 90% sequence homology to the polypeptide sequence of SEQ ID NO: 2 would not be possible. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (guided mutants). Such guidance has **not** been provided in the instant specification.

Therefore, the specification does not support the broad scope of the claims which encompass: i) any nucleic acid molecule encoding a polypeptide having α-1,6-mannosyltransferase activity and comprising an amino acid sequence having at least 90% homology to the amino acid sequence of SEQ ID NO: 2 (as in claims 1-3); and ii) an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern (as in claims 4-11), because the specification does not establish: (A) regions of the protein/polynucleotide structure which may be modified without affecting the activity of encoded α-1,6-mannosyltransferase activity; (B) the general tolerance of the polypeptide and the polynucleotide encoding α-1,6-mannosyltransferase activity to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; (D)

an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme of undefined structure and associated function including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claim broadly including polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1975)). Without sufficient guidance, determination of polypeptides having the desired biological/enzymological/physicochemical characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention. Claim 4 recites a recombinant vector comprising the nucleic acid molecule of SEQ ID NO: 1 deposited under accession number KCTC 10583BP and claim 5 recites *Hansenula polymorpha Hpoch2Δ* mutant strain deposited under accession number KCTC 10584BP.

It is apparent that a recombinant vector comprising the nucleic acid molecule of SEQ ID NO: 1 deposited under accession number KCTC 10583BP and *Hansenula polymorpha Hpoch2Δ* mutant strain deposited under accession number KCTC 10584BP are required to practice the claimed invention. As such the biological material must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 USC112, first paragraph, may be satisfied by a deposit of a recombinant vector comprising the nucleic acid molecule of SEQ ID NO: 1 deposited under accession number KCTC 10583BP and *Hansenula polymorpha Hpoch2Δ* mutant strain deposited under accession number KCTC 10584BP1. The specification does not disclose a repeatable method to obtain a recombinant vector comprising the nucleic acid molecule of SEQ ID NO: 1 deposited under accession number KCTC 10583BP and *Hansenula polymorpha Hpoch2Δ* mutant strain deposited under accession number KCTC 10584BP. It is noted that applicants have deposited the a recombinant vector comprising the nucleic acid molecule of SEQ ID NO: 1 deposited under accession number KCTC 10583BP and *Hansenula polymorpha Hpoch2Δ* mutant strain deposited under accession number KCTC 10584BP on 01/15/2007 with the Korean Collection for Type Cultures, #52, Oun-dong, Yusong-ku, Taejon 305-333, Korea (pages 11, 29 and

30 of specification), but there is no indication in the specification as to the public availability or the deposit was made under the terms of Budapest Treaty. A statement, affidavit or declaration by Applicants, or a statement by an attorney of record over his/her signature and registration number, or someone empowered to make such a statement, stating that the invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. In order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, applicant may provide assurance of compliance by statement, affidavit or declaration, or by someone empowered to make same, or by a statement by an attorney of record over his /her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting the patent;

(c) the deposit will be maintained in public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (se 37 CFR 1.807); and the deposit will be replaced if it should ever become inviable.

Written Description

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-11 as interpreted are directed to encompass: i) any nucleic acid molecule encoding a polypeptide having α-1,6-mannosyltransferase activity and comprising an amino acid sequence having at least 90% homology to the amino acid sequence of SEQ ID NO: 2 (as in claims 1-3); and ii) an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern (as in claims 4-11).

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In the instant case the scope of the instant claims encompass a genus of structures (no structural limitation) for polypeptides of interest, i.e., i) any nucleic acid

molecule encoding a polypeptide having α-1,6-mannosyltransferase activity and comprising an amino acid sequence having at least 90% homology to the amino acid sequence of SEQ ID NO: 2 (as in claims 1-3); and ii) an engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising any polynucleotide sequence encoding any sugar-chain modifying enzyme including variants, mutants and recombinants capable of producing/glycosylating any glycoprotein with reduction in any undefined glycosylation pattern (as in claims 4-11).

No information, beyond the characterization of an isolated polypeptide having α-1,6-mannosyltransferase activity and comprising the amino acid sequence of SEQ ID NO: 2 and encoded by a polynucleotide of SEQ ID NO: 1; a specific *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP) transfected with an expression vector comprising polynucleotide sequence encoding a α-1,2-mannosidase having the activity of synthesizing sugar chains with 5 or 6 mannose residues, said polynucleotide sequence isolated from the nucleic acid of *Aspergillus saitoi* by PCR amplification using the primers of SEQ ID NO: 13 (forward primer) and SEQ ID NO: 14 (reverse primer) and said engineered *Hansenula polymorpha Hpoch2Δ* mutant strain (KCTC 10584BP; comprising a specific mutation) transfected with an expression vector comprising polynucleotide sequence encoding a α-1,2-mannosidase capable of producing glycoproteins comprising human mannose-type N-glycan (Example 5, pages 24-27 of specification), has been provided by the applicants, which would indicate that they had

possession of the claimed genus of structures (no structural limitation) for polypeptides of interest.

The art also teaches, even highly structurally homologous polypeptides do not necessarily share the same function and conversely functionally similar molecules do not necessarily have similar structures. For example proteins having similar structure have different activities; Witkowski et al., (Biochemistry 38:11643-11650, 1999) teaches that one conservative amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Similarly, Wishart et al., (J. Biol. Chem., 1995, Vol. 270(10): 26782-26785) teach that a single mutation converts a novel phosphotyrosine binding domain into a dual-specificity phosphatase. The art also teaches that functionally similar molecules have different structures; Kisselev L., (Structure, 2002, Vol. 10: 8-9) teach that polypeptide release factors in prokaryotes and eukaryotes have same function but different structures.

Hence, the recited genera polypeptides and encoding polynucleotides are interpreted to have widely variable structures, since minor changes may result in changes affecting function and no additional information correlating structure with function has been provided.

Therefore, given the lack of description of representative species encompassed by the genus of polynucleotides and encoded polypeptides and modifications, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicants are referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Allowable Subject Matter/Conclusion

None of the claims are allowed.

Art of Interest

Kim et al, (J. Biol. Chem., March 10, 2006, Vol. 281 (10): 6261-6272) disclose an isolated polypeptide having α-1,6-mannosyltransferase activity and encoding polynucleotide having 100% sequence homology to SEQ ID NO: 1 and SEQ ID NO: 2 of the instant invention. However, the cited art is not used in any rejection as this is the work of applicants' group that is published after the effective filing date of the instant invention.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathirama Raghu/
Patent Examiner
Art Unit 1652.